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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/491,974	01/27/2000	Connie S. Schmaljohn	003/115/SAP RIID96-10	9304

7590 03/05/2003

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EXAMINER
WOITACH, JOSEPH T

ART UNIT	PAPER NUMBER
1632	

DATE MAILED: 03/05/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

File

Advisory Action

Application No.	Applicant(s)
09/491,974	Schmaljohn et al.
Examiner	**Art Unit**
Joseph Woitach	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED *Feb 10, 2003* FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid the abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

THE PERIOD FOR REPLY [check only a) or b)]

a) ☒ The period for reply expires *3* months from the mailing date of the final rejection.

b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on _____. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.

2. ☐ The proposed amendment(s) will not be entered because:

(a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);

(b) ☐ they raise the issue of new matter (see NOTE below);

(c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or

(d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: _____

3. ☐ Applicant's reply has overcome the following rejection(s):

4. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).

5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See attached.

6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.

7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: *46 and 47*

Claim(s) objected to: *33, 34, 42, 43, 50, and 51*

Claim(s) rejected: *28-32, 35-41, 44, 45, 48, and 49*

Claim(s) withdrawn from consideration: _____

8. ☐ The proposed drawing correction filed on _____ is a) ☐ approved or b) ☐ disapproved by the Examiner.

9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____.

10. ☐ Other:

Deborah Crouch

DEBORAH CROUCH
PRIMARY EXAMINER
GROUP 1800/1630

Section 5(c):

Applicants note the amendments to the claims and argue that there is no teaching in any of the references that vaccinia virus vaccines would predict efficacy of DNA vaccines (page 2-3). Initially, Applicants acknowledge that Schmaljohn *et al.* provide evidence that hantavirus gene products are immunogenic and that Donnelly and Montgomery teach that DNA vaccines are safer and more flexible than vaccinia vectors. However, first, Applicants argue that vaccinia virus replicates in the cytoplasm versus DNA vaccines which require delivery to the nucleus for transcription. This argument is not found persuasive because it is well known in the art that polynucleotides delivered to a cell are actively taken-up, transcribed and translated to produce proteins. The difference on how a protein/antigen is produced either starting in the nucleus with host cell factors or in the cytoplasm by a live vaccinia virus are immaterial to the protein produced or its ability to serve as an antigen. Additionally, Applicants argue that Hantaan virus transcripts contain cryptic splice sites that pose potential problems for host cell factors to process. Note that obviousness does not require absolute predictability of success; for obviousness under 35 U.S.C. § 103, all that is required is a reasonable expectation of success. See *In re O'Farrell*, 7 USPQ2d 1673 (CAFC 1988). Applicants' argument is not found persuasive because the proteins have been generated by other expression systems besides vaccinia (as acknowledged in the specification (page2)) and any 'potential' problem appears to be mute in light of evidence for expression in both prokaryote and eukaryote. Second, Applicants argue that the invention is a novel composition and is critical requirement to for effectiveness of the method (page 3). This

argument is not persuasive because as discussed above given that Schmaljohn *et al.* provide evidence that hantavirus proteins are immunogenic and Donnelly and Montgomery teach that DNA vaccines are safer and more flexible than vaccinia vectors, the claimed composition would have been obvious and not novel. Once a protein antigen is produced the ability of hantavirus proteins to serve as an antigen would be inherent as evidenced by Schmaljohn *et al.* There is no 'critical' element to the instantly claimed polynucleotide which would distinguish it from that disclosed by Donnelly or Montgomery. Finally, Applicants' note that if a vaccinia viral vector was delivered alone it would not be effective because it would require viral factors the host cell may not contain (page 3). Examiner agrees with Applicants final point, however it is noted that claim 28 has been now been amended and that the original claim was drawn simply to a composition comprising an inert particle and a polynucleotide encoding a hantavirus protein and did not require that the polynucleotide to be expressed in any specific context.

Applicants' summarize that it only becomes "obvious" that a DNA vaccine will work after it is shown that (1) the DNA can get to the nucleus, (2) the DNA can be transcribed to yield mRNA, and (3) the RNA transcripts get out of the nucleus and move to the cytoplasm where they can be translated into a protein antigen. Applicants' arguments have been fully considered but not found persuasive because these three factors were clearly know at the time of filing. Moreover, the ability to deliver a polynucleotide to express a protein of interest was well known in the art and used to express a wide variety of proteins from various sources. There is nothing unique to the instantly claimed composition than that made obvious by the teaching of Donnelly

et al. and Montgomery *et al.* Schmaljohn *et al.* and Arikawa *et al.* It must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971). In the instant case, Applicants do not contest and acknowledge that Schmaljohn *et al.* provide evidence that hantavirus gene products are immunogenic and that Donnelly *et al.* and Montgomery *et al.* teach that DNA vaccines are safer and more flexible than vaccinia vectors (see amendment page 2) which anticipate each of the elements of the claims. Further, Donnelly *et al.* and Montgomery *et al.* clearly teach that DNA vaccines have been used to express other antigens and given that Schmaljohn *et al.* provide evidence that Hantaan viral proteins serve as effective protein antigens when expressed by other vectors there would have been a reasonable expectation of success to use a DNA vaccine to express Hantaan viral proteins.

Therefore, for the reasons above and of record, the rejection is maintained.